

WE CLAIM:

1. A method of binding the imidazoline receptor, comprising:
contacting a bis-benzene to said imidazoline receptor in an amount effective to
5 bind to said receptor, wherein said bis-benzene contains at least one amidine group.

2. A method according to claim 1, wherein said contacting step is carried out
in vitro.

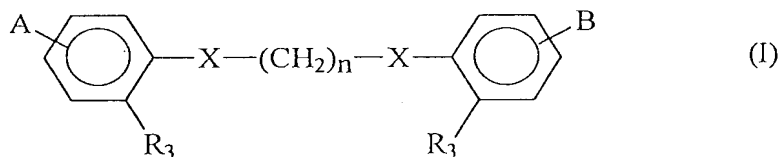
10 3. A method according to claim 1, wherein said contacting step is carried out
in vitro with cells that express said imidazoline receptor.

4. A method according to claim 1, wherein said contacting step is carried out
in vitro with a cell-free preparation comprising said imidazoline receptor.

15 5. A method according to claim 1, wherein said contacting step is carried out
in vivo.

20 6. A method according to claim 1, wherein said contacting step is carried out
in vivo by administering said compound to a subject afflicted with a disease state
which is alleviable by treatment with a compound having high selectivity and affinity for
the imidazoline receptor site.

25 7. A method according to claim 1, wherein said bis-benzene has the formula I:



30 wherein:

A and B are each independently selected from the group consisting of H, loweralkyl, oxyalkyl, nitro, amino, aminoalkyl, halo, hydroxy, carboxy, and compounds of formula (i):



10 subject to the proviso that at least one of A and B is a compound of formula (i);

R₁ and R₂ are each independently selected from the group consisting of H, loweralkyl, oxyalkyl, alkoxyalkyl, cyloalkyl, aryl, hydroxyalkyl, aminoalkyl and alkylaminoalkyl; or two R₁ group on the same amidine group together represent – (CH₂)_m– wherein m is 2, 3, or 4;

15 R₃ is H, loweralkyl, oxyalkyl, alkoxyalkyl, hydroxyalkyl, cycloalkyl, aryl, aminoalkyl, alkylaminoalkyl or halogen;

n is from 2 to 6; and

X is O, NH, or S;

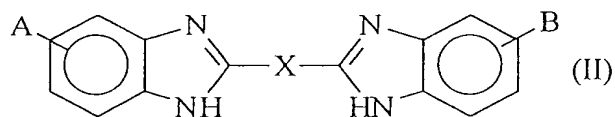
or a pharmaceutically acceptable salt thereof.

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8. A method according to claim 7, wherein R₁, R₂ and R₃ are H; wherein X is O; and wherein n is 5.

9. A method according to claim 1, wherein said bis-benzene has the formula

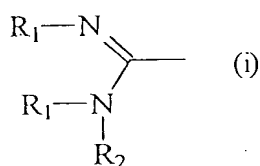
25 II:



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wherein:

A and B are each independently selected from the group consisting of H, loweralkyl, oxyalkyl, nitro, amino, aminoalkyl, halo, hydroxy, carboxy, and compounds of formula (i):

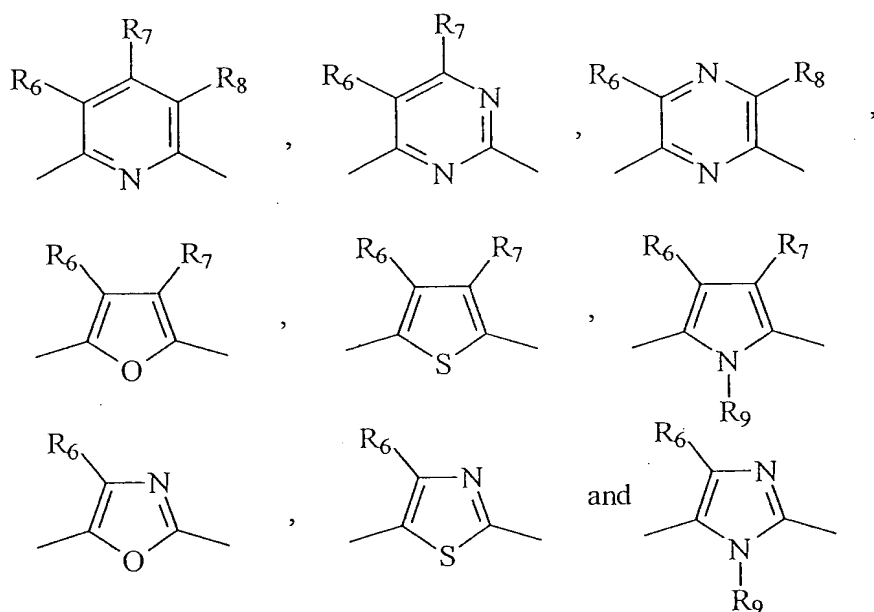


subject to the proviso that at least one of A and B is a compound of formula (i);

R₁ and R₂ are each independently selected from the group consisting of H, loweralkyl, oxyalkyl, alkoxyalkyl, cyloalkyl, aryl, hydroxyalkyl, aminoalkyl and alkylaminoalkyl; or two R₁ group on the same amidine group together represent – (CH₂)_m– wherein m is 2, 3, or 4;

R₃ is H, loweralkyl, oxyalkyl, alkoxyalkyl, hydroxyalkyl, cycloalkyl, aryl, aminoalkyl, alkylaminoalkyl or halogen;

X is linear or branched, saturated or unsaturated C1-C12 alkyl containing up to 4 double bonds; or X is a heterocyclic aromatic group selected from the group consisting of:



wherein

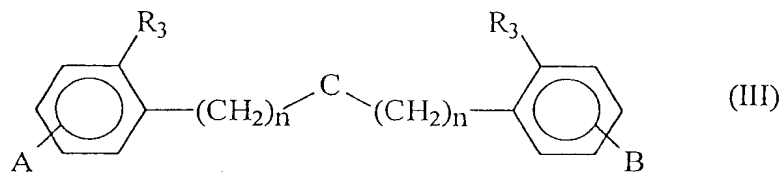
R₆, R₇, and R₈ are each independently selected from the group consisting of H, loweralkyl, halogen, oxyalkyl, oxyaryl, or oxyarylalkyl;

R₉ is hydrogen, loweralkyl, hydroxy, aminoalkyl or alkylaminoalkyl;

or the pharmaceutically acceptable salts thereof.

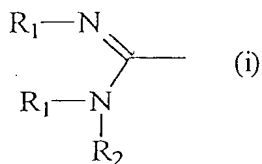
10. A method according to claim 1, wherein said bis-benzene has the formula

III:



10
wherein:

A and B are each independently selected from the group consisting of H, loweralkyl, oxyalkyl, nitro, amino, aminoalkyl, halo, hydroxy, carboxy, and substituents of formula (i):

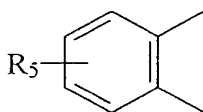


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subject to the proviso that at least one of A and B is a substituent of formula (i);

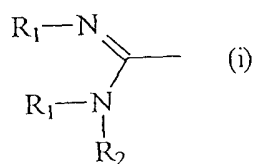
R₁ and R₂ are each independently selected from the group consisting of H, loweralkyl, oxyalkyl, alkoxyalkyl, cyloalkyl, aryl, hydroxyalkyl, aminoalkyl and alkylaminoalkyl; or two R₁ groups on the same amidine group together represent –
25 (CH₂)_m– wherein m is 2, 3, or 4;

R₃ is H, loweralkyl, oxyalkyl, alkoxyalkyl, hydroxyalkyl, cycloalkyl, aryl, aminoalkyl, alkylaminoalkyl or halogen;

or two R₁ groups on the same amidine group together represent

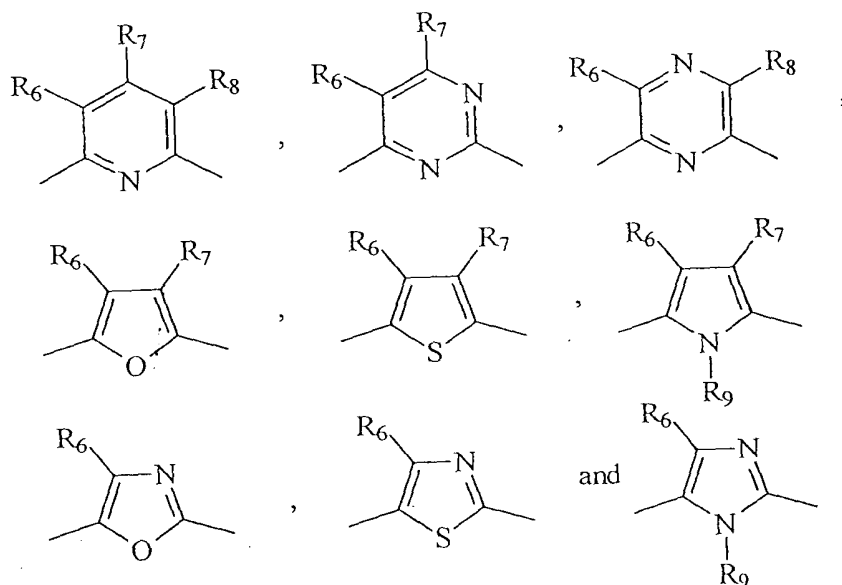


wherein R_5 is



n is an integer from 0 to 2; and

A is a heterocyclic aromatic group selected from the group consisting of:

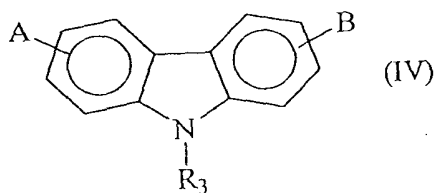


wherein

R_6 , R_7 , and R_8 are each independently selected from the group consisting of H, loweralkyl, halogen, oxyalkyl, oxyaryl, or oxyarylalkyl;

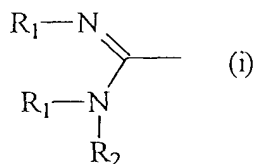
R_9 is hydrogen, loweralkyl, hydroxy, aminoalkyl or alkylaminoalkyl; and the pharmaceutically acceptable salts thereof.

11. A method according to claim 1, wherein said bis-benzamidine has the formula IV:



wherein:

A and B are each independently selected from the group consisting of H, loweralkyl, oxyalkyl, nitro, amino, aminoalkyl, halo, hydroxy, carboxy, and substituents of formula (i):

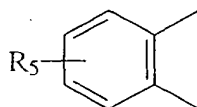


subject to the proviso that at least one of A and B is a substituent of formula (i);

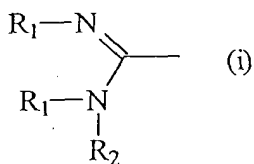
10 R_1 and R_2 are each independently selected from the group consisting of H, loweralkyl, oxyalkyl, alkoxyalkyl, cyloalkyl, aryl, hydroxyalkyl, aminoalkyl and alkylaminoalkyl; or two R_1 group on the same amidine group together represent $-(CH_2)_m-$ wherein m is 2, 3, or 4;

R_3 is H, loweralkyl, oxyalkyl, alkoxyalkyl, hydroxyalkyl, cycloalkyl, aryl, 15 aminoalkyl, alkylaminoalkyl or halogen;

or two R_1 groups on the same amidine group together represent

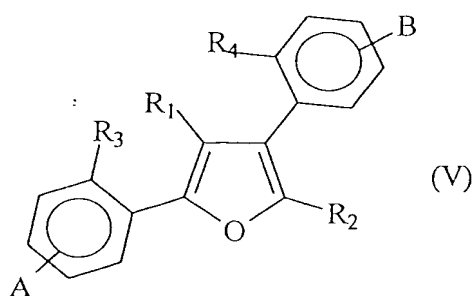


wherein R_5 is



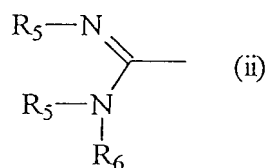
and the pharmaceutically acceptable salts thereof.

12. A method according to claim 1, said bis-benzene having the formula (V):



wherein:

A and B are each independently selected from the group consisting of H, loweralkyl, oxyalkyl, nitro, amino, aminoalkyl, halo, hydroxy, carboxy, and substituents of formula (ii):



subject to the proviso that at least one of A and B is a substituent of formula (ii);

R₁ and R₂ are each independently selected from the group consisting of H, loweralkyl, aryl, alkylaryl, aminoalkyl, aminoaryl, halogen, oxyalkyl, oxyaryl, or oxyarylalkyl;

25 R₃ and R₄ are each independently selected from the group consisting of H, loweralkyl, oxyalkyl, alkylaryl, aryl, oxyaryl, aminoalkyl, aminoaryl, or halogen; and

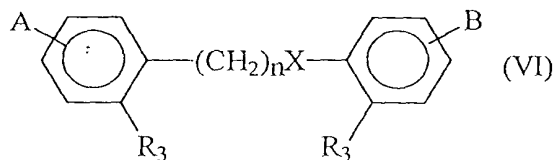
each R₅ is independently selected from the group consisting of H, loweralkyl, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, cycloalkyl, aryl, or alkylaryl or two R₅ groups together represent C₂ to C₁₀ alkyl, hydroxyalkyl, or alkylene; and

30 R₆ is H, hydroxy, loweralkyl, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylamino, alkylaminoalkyl, cycloalkyl, hydroxycycloalkyl, alkoxycycloalkyl, aryl, or alkylaryl;

or a pharmaceutically acceptable salt thereof.

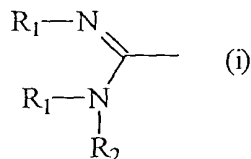
13. A method according to claim 1, wherein said bis-benzene has the formula

VI:



wherein:

A and B are each independently selected from the group consisting of H,
10 loweralkyl, oxyalkyl, nitro, amino, aminoalkyl, halo, hydroxy, carboxy, and
substituents of formula (i):

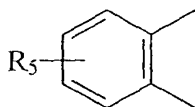


subject to the proviso that at least one of A and B is a substituent of formula (i);

R₁ and R₂ are each independently selected from the group consisting of H,
loweralkyl, oxyalkyl, alkoxyalkyl, cyloalkyl, aryl, hydroxyalkyl, aminoalkyl and
20 alkylaminoalkyl; or two R₁ group on the same amidine group together represent
(CH₂)_m- wherein m is 2, 3, or 4;

R₃ is H, loweralkyl, oxyalkyl, alkoxyalkyl, hydroxyalkyl, cycloalkyl, aryl,
aminoalkyl, alkylaminoalkyl or halogen;

or two R₁ groups on the same amidine group together represent



wherein R₅ is

